

**WHAT IS CLAIMED IS:**

1. A method for simultaneously treating mucositis and fungal infection in a mammal in need thereof, said method comprising administering to said mammal an effective amount of an anti-mucositis and anti-fungal pharmaceutical composition consisting of a tetracycline compound in an amount that is effective to simultaneously treat mucositis and fungal infection, but has substantially no antibiotic activity.
2. A method according to Claim 1 wherein said fungus is selected from the group consisting of *Cryptococcus* species, *Candida albicans*, *Rhizopus* species, *Aspergillus fumigatus*, *Penicillium* species, *Absidia* species, *Scedosporium apiospermum*, *Phialophora verrucosa*, *Cunninghamella* species, *Tricothecium* species, *Ulocladium* species, *Fonsecae* species, and combinations thereof.
3. A method according to Claim 1 wherein said fungus is selected from the group consisting of *Rhizopus* species, *Absidia* species, *Scedosporium apiospermum*, *Phialophora verrucosa*, *Cunninghamella* species, *Tricothecium* species, *Ulocladium* species, *Fonsecae* species, or a combination thereof, and wherein said non-antibiotic tetracycline derivative is CMT-3.
4. A method according to Claim 1 wherein said fungus is *Aspergillus fumigatus*, *Penicillium* species, *Rhizopus* species, *Candida albicans*, or a combination thereof, and wherein said non-antibiotic tetracycline derivative is CMT-315.
5. A method according to Claim 1 wherein said fungus is *Penicillium* species and said non-antibiotic tetracycline derivative is CMT-4.
6. A method according to Claim 1 wherein said fungus is *Candida albicans* and said non-antibiotic tetracycline derivative is CMT-7.
7. A method according to Claim 1 wherein said fungus is *Aspergillus fumigatus*, *Penicillium* species or a combination thereof, and said non-antibiotic is CMT-308.

8. A method according to Claim 1 wherein said fungus is *Penicillium* species, *Scedosporium apiospermum*, *Tricothecium* species, *Ulocladium* species, or a combination thereof and said non-antibiotic tetracycline derivative is CMT-8.
9. A method according to Claim 1 wherein said mammal is a human.
10. A method according to Claim 1 wherein said treatment comprises administering said non-antibiotic tetracycline derivative systemically.
11. A method according to Claim 10, wherein said systemic administration is oral administration, intravenous injection, intramuscular injection, subcutaneous administration, transdermal administration or intranasal administration.
12. A method according to Claim 1, wherein said tetracycline compound is an antibiotic tetracycline compound administered in an amount which is 10-80% of the antibiotic amount.
13. A method according to Claim 1, wherein said tetracycline compound is doxycycline administered twice a day in a dose of 20 mg.
14. A method according to Claim 1, wherein said tetracycline compound is minocycline administered once a day in a dose of 38 mg.
15. A method according to Claim 1, wherein said tetracycline compound is minocycline administered twice a day in a dose of 38 mg.
16. A method according to Claim 1, wherein said tetracycline compound is minocycline administered three times a day in a dose of 38 mg.
17. A method according to Claim 1, wherein said tetracycline compound is tetracycline administered twice a day in a dose of 60 mg/day.

18. A method according to Claim 1, wherein said tetracycline compound is tetracycline administered three times a day in a dose of 60 mg/day.
19. A method according to Claim 1, wherein said tetracycline compound is tetracycline administered four times a day in a dose of 60 mg/day.
20. A method according to Claim 1, wherein said tetracycline compound is an antibiotic tetracycline compound administered in an amount which results in a serum concentration which is 10-80% of the minimum antibiotic serum concentration.
21. A method according to Claim 1, wherein said tetracycline compound is doxycycline administered in an amount which results in a serum concentration which is 1.0  $\mu\text{g/ml}$ .
22. A method according to Claim 1, wherein said tetracycline compound is minocycline administered in an amount which results in a serum concentration which is 0.8  $\mu\text{g/ml}$ .
23. A method according to Claim 1, wherein said tetracycline compound is tetracycline administered in an amount which results in a serum concentration which is 0.5  $\mu\text{g/ml}$ .
24. A method according to Claim 12 or 20, wherein said antibiotic tetracycline compound is doxycycline, minocycline, tetracycline, oxytetracycline, chlortetracycline, demeclocycline or pharmaceutically acceptable salts thereof.
25. A method according to Claim 24, wherein said antibiotic tetracycline compound is doxycycline.
26. A method according to Claim 25, wherein said doxycycline is administered in an amount which provides a serum concentration in the range of about 0.1 to about 0.8  $\mu\text{g/ml}$ .

27. A method according to Claim 25, wherein said doxycycline is administered in an amount of 20 milligrams twice daily.

28. A method according to Claim 26, wherein said doxycycline is administered by sustained release over a 24 hour period.

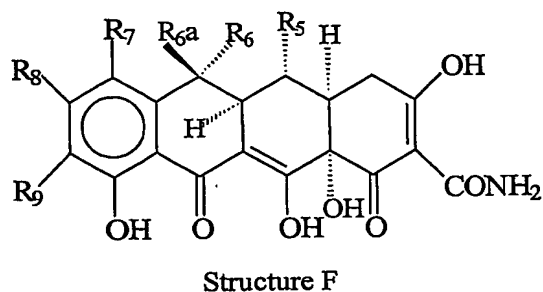
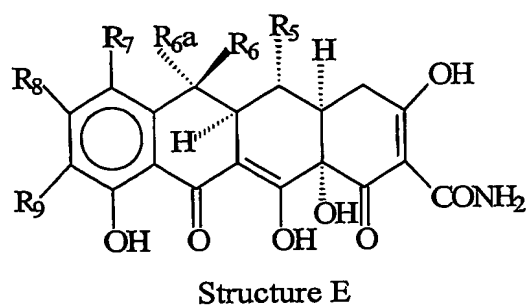
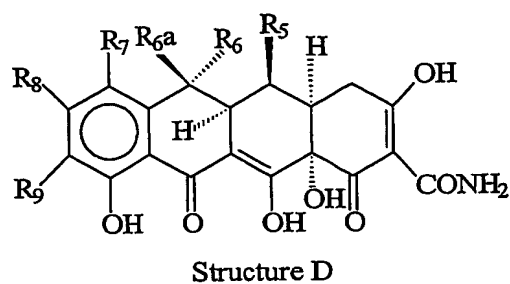
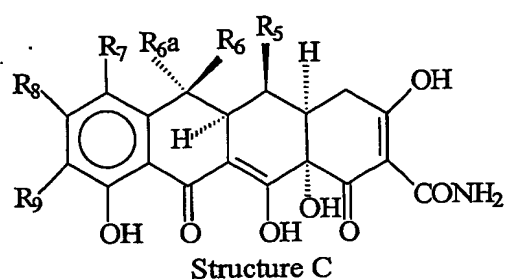
29. A method according to Claim 28, where said doxycycline is administered in an amount of 40 milligrams.

30. A method according to Claim 1, wherein said tetracycline compound is a non-antibiotic tetracycline compound.

31. A method according to Claim 30, wherein said non-antibiotic tetracycline compound is:

4-de(dimethylamino)tetracycline (CMT-1),  
tetracyclonitrile (CMT-2),  
6-demethyl-6-deoxy-4-de(dimethylamino)tetracycline (CMT-3),  
4-de(dimethylamino)-7-chlorotetracycline (CMT-4),  
tetracycline pyrazole (CMT-5)  
4-hydroxy-4-de(dimethylamino)tetracycline (CMT-6),  
4-de(dimethylamino)-12 $\alpha$ -deoxytetracycline (CMT-7),  
6- $\alpha$ -deoxy-5-hydroxy-4-de(dimethylamino)tetracycline (CMT-8),  
4-de(dimethylamino)-12 $\alpha$ -deoxyanhydrotetracycline (CMT-9), or  
4-de(dimethylamino)minocycline (CMT-10).

32. A method according to Claim 30, wherein the non-antibiotic tetracycline compound is selected from the group consisting of:



wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, mono(lower alkyl) amino, halogen, di(lower alkyl)amino, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

R6 and R5 are selected from the group consisting of hydrogen and hydroxyl;

R8 is selected from the group consisting of hydrogen and halogen;

R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, mono(lower alkyl) amino, halogen, diazonium, di(lower alkyl)amino and  $RCH(NH_2)CO$ ;

R is hydrogen or lower alkyl; and

pharmaceutically acceptable salts thereof; with the following provisos:

when either R7 and R9 are hydrogen then R8 must be halogen; and

when R6-a, R6, R5 and R9 are all hydrogen and R7 is hydrogen, amino, nitro, halogen, dimethylamino or diethylamino, then R8 must be halogen; and

when R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl, and R7 is hydrogen, amino, nitro, halogen or diethylamino, then R8 is halogen; and

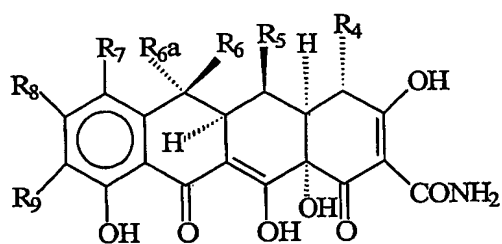
when R6-a is methyl, R6 is hydroxyl, R5, R7 and R9 are all hydrogen, then R8 must be halogen; and

when R6-a, R6 and R5 are all hydrogen, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

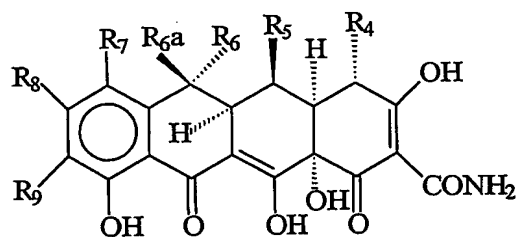
when R6-a is methyl, R6 is hydrogen, R5 is hydroxyl, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

when R6-a is methyl, R6, R5 and R9 are all hydrogen and R7 is cyano, then R8 must be halogen.

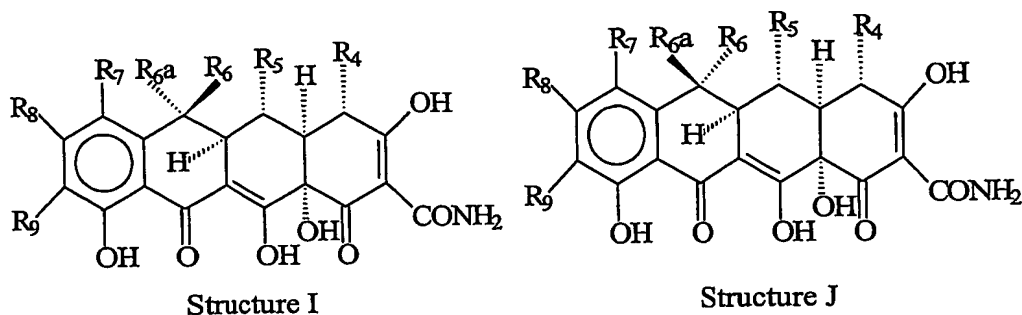
33. A method according to Claim 30, wherein the non-antibiotic tetracycline compound is selected from the group consisting of:



### Structure G



### Structure H



wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, mono(lower alkyl) amino, halogen, and di(lower alkyl)amino, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

R6 and R5 are selected from the group consisting of hydrogen and hydroxyl;

R4 is selected from the group consisting of NOH, N-NH-A, and NH-A, where A is a lower alkyl group;

R8 is selected from the group consisting of hydrogen and halogen;

R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, mono(lower alkyl) amino, halogen, di(lower alkyl)amino and  $RCH(NH_2)CO$ ;

R is hydrogen or lower alkyl; and

pharmaceutically acceptable salts thereof; with the following provisos:

when R4 is NOH, N-NH-alkyl or NH-alkyl and R7, R6-a, R6, R5, and R9 are all hydrogen, then R8 must be halogen; and

when R4 is NOH, R6-a is methyl, R6 is hydrogen or hydroxyl, R7 is halogen, R5 and R9 are both hydrogen, then R8 must be halogen; and

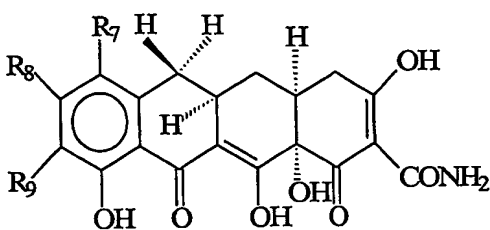
when R4 is N-NH-alkyl, R6-a is methyl, R6 is hydroxyl and R7, R5, R9 are all hydrogen, then R8 must be halogen; and

when R4 is NH-alkyl, R6-a, R6, R5 and R9 are all hydrogen, R7 is hydrogen, amino, mono(lower alkyl)amino, halogen, di(lower alkyl)amino or hydroxyl, then R8 must be halogen; and

when R4 is NH-alkyl, R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl, and R7 is mono(lower alkyl)amino or di(lower alkyl)amino, then R8 must be halogen; and

when R4 is NH-alkyl, R6-a is methyl, R6 is hydroxy or hydrogen and R7, R5, and R9 are all be hydrogen, then R8 must be halogen.

34. A method according to Claim 30 wherein the non-antibiotic tetracycline compound is selected from the group consisting of:



Structure K

wherein: R7, R8, and R9 taken together in each case, have the following meanings:

R7	R8	R9
azido	hydrogen	hydrogen
dimethylamino	hydrogen	azido
hydrogen	hydrogen	amino
hydrogen	hydrogen	azido
hydrogen	hydrogen	nitro
dimethylamino	hydrogen	amino
acylamino	hydrogen	hydrogen
hydrogen	hydrogen	acylamino
amino	hydrogen	nitro
hydrogen	hydrogen	(N,N-dimethyl)glycylamino
amino	hydrogen	amino
hydrogen	hydrogen	ethoxythiocarbonylthio
dimethylamino	hydrogen	acylamino
dimethylamino	hydrogen	diazonium
dimethylamino	chloro	amino
hydrogen	chloro	amino
amino	chloro	amino
acylamino	chloro	acylamino
amino	chloro	hydrogen

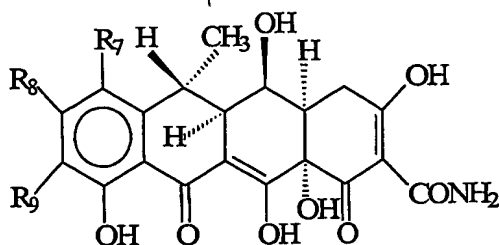


acylamino  
monoalkylamino  
nitro  
dimethylamino  
dimethylamino  
hydrogen  
dimethylamino

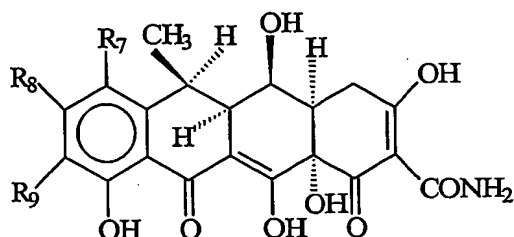
chloro  
chloro  
chloro  
chloro  
hydrogen  
hydrogen

hydrogen  
amino  
amino  
acylamino  
dimethylamino  
dimethylamino  
hydrogen

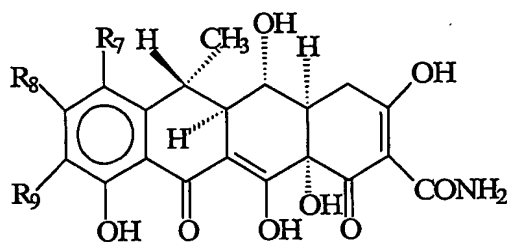
and



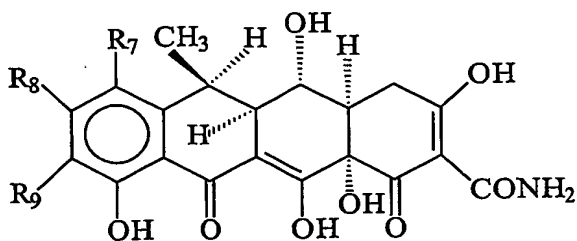
Structure L



Structure M



Structure N



Structure O

wherein: R7, R8, and R9 taken together in each case, have the following meanings:

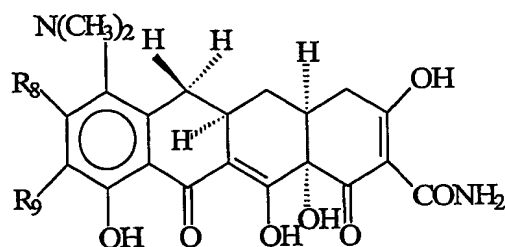
R7  
azido  
dimethylamino  
hydrogen

R8  
hydrogen  
hydrogen  
hydrogen

R9  
hydrogen  
azido  
amino

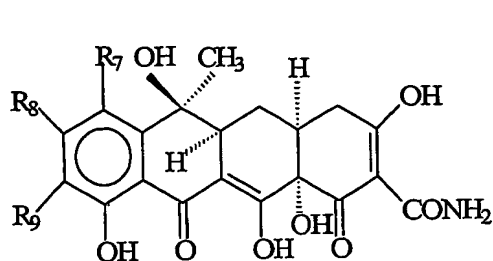
hydrogen	hydrogen	azido
hydrogen	hydrogen	nitro
dimethylamino	hydrogen	amino
acylamino	hydrogen	hydrogen
hydrogen	hydrogen	acylamino
amino	hydrogen	nitro
hydrogen	hydrogen	(N,N-dimethyl)glycylamino
amino	hydrogen	amino
hydrogen	hydrogen	ethoxythiocarbonylthio
dimethylamino	hydrogen	acylamino
hydrogen	hydrogen	diazonium
hydrogen	hydrogen	dimethylamino
diazonium	hydrogen	hydrogen
ethoxythiocarbonylthio	hydrogen	hydrogen
dimethylamino	chloro	amino
amino	chloro	amino
acylamino	chloro	acylamino
hydrogen	chloro	amino
amino	chloro	hydrogen
acylamino	chloro	hydrogen
monoalkylamino	chloro	amino
nitro	chloro	amino

and

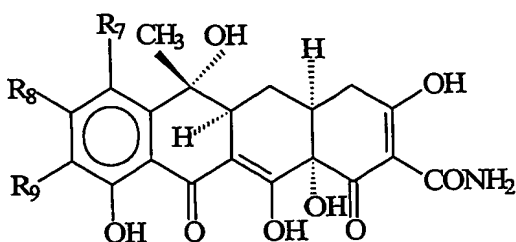


Structure P

wherein: R8 is hydrogen or halogen and R9 is selected from the group consisting of nitro, (N,N-dimethyl)glycylamino, and ethoxythiocarbonylthio; and



Structure Q



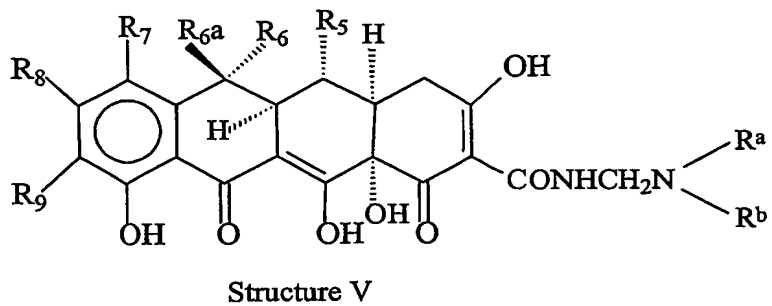
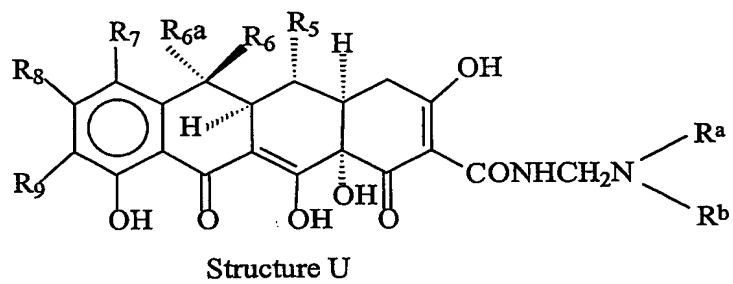
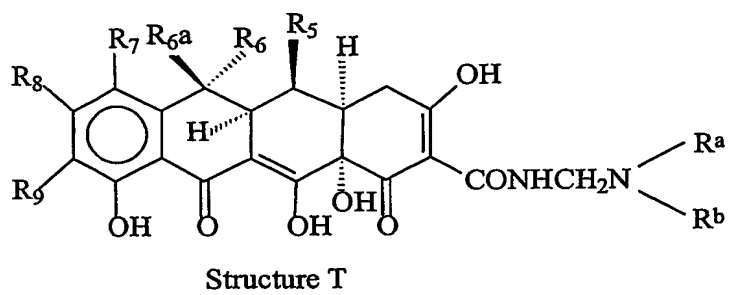
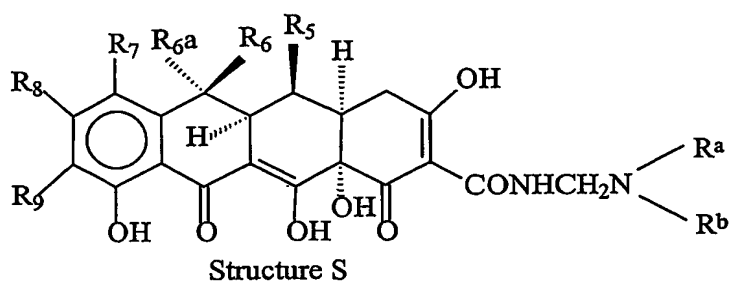
Structure R

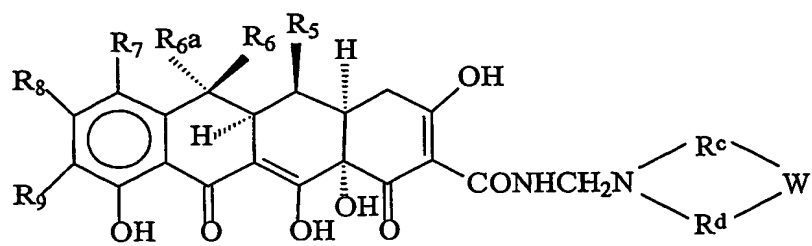
wherein: R7, R8, and R9 taken together in each case, have the following meanings:

R7	R8	R9
amino	hydrogen	hydrogen
nitro	hydrogen	hydrogen
azido	hydrogen	hydrogen
dimethylamino	hydrogen	azido
hydrogen	hydrogen	amino
hydrogen	hydrogen	azido
hydrogen	hydrogen	nitro
bromo	hydrogen	hydrogen
dimethylamino	hydrogen	amino
acylamino	hydrogen	hydrogen
hydrogen	hydrogen	acylamino
amino	hydrogen	nitro
hydrogen	hydrogen	(N,N-dimethyl)glycylamino
amino	hydrogen	amino
diethylamino	hydrogen	hydrogen
hydrogen	hydrogen	ethoxythiocarbonylthio
dimethylamino	hydrogen	methylamino
dimethylamino	hydrogen	acylamino
dimethylamino	chloro	amino
amino	chloro	amino
acylamino	chloro	acylamino
hydrogen	chloro	amino
amino	chloro	hydrogen
acylamino	chloro	hydrogen
monoalkylamino	chloro	amino
nitro	chloro	amino

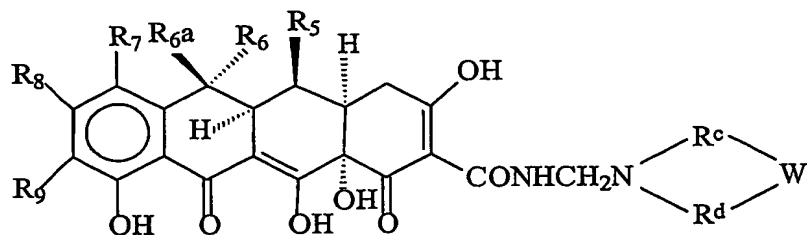
and pharmaceutically acceptable salts thereof.

35. A method according to Claim 30, wherein the non-antibiotic tetracycline compound is selected from the group consisting of:

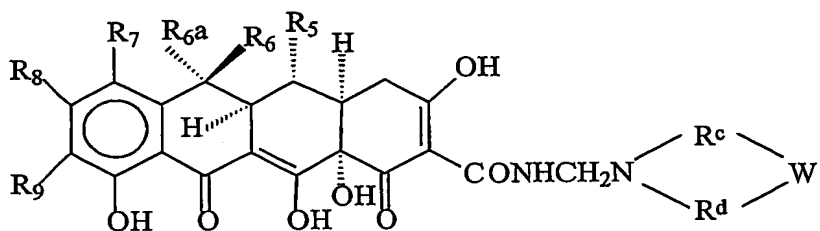




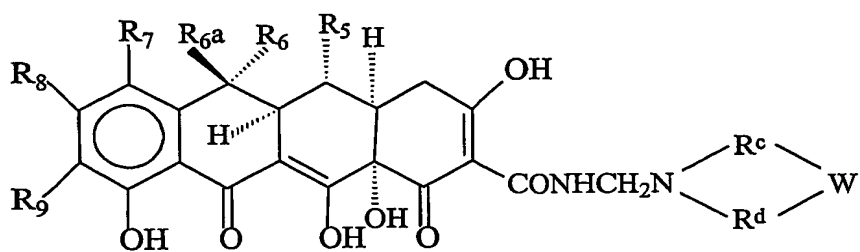
Structure W



Structure X



Structure Y



Structure Z

wherein:

R7 is selected from the group consisting of hydrogen, amino, nitro, mono(lower alkyl) amino, halogen, di(lower alkyl)amino, ethoxythiocarbonylthio, azido, acylamino, diazonium, cyano, and hydroxyl;

R6-a is selected from the group consisting of hydrogen and methyl;

R6 and R5 are selected from the group consisting of hydrogen and hydroxyl;

R8 is selected from the group consisting of hydrogen and halogen;

R9 is selected from the group consisting of hydrogen, amino, azido, nitro, acylamino, hydroxy, ethoxythiocarbonylthio, mono(lower alkyl) amino, halogen, diazonium, di(lower alkyl)amino and  $\text{RCH}(\text{NH}_2)\text{CO}$ ;

R is hydrogen or lower alkyl;

$\text{R}^a$  and  $\text{R}^b$  are selected from the group consisting of hydrogen, methyl, ethyl, n-propyl and 1-methylethyl with the proviso that  $\text{R}^a$  and  $\text{R}^b$  cannot both be hydrogen;

$\text{R}^c$  and  $\text{R}^d$  are, independently,  $(\text{CH}_2)_n\text{CHR}^e$  wherein n is 0 or 1 and  $\text{R}^e$  is selected from the group consisting of hydrogen, alkyl, hydroxy, lower( $\text{C}_1\text{-C}_3$ ) alkoxy, amino, or nitro; and,

W is selected from the group consisting of  $(\text{CHR}^e)_m$  wherein m is 0-3 and said  $\text{R}^e$  is selected from the group consisting of hydrogen, alkyl, hydroxyl, lower( $\text{C}_1\text{-C}_3$ ), alkoxy, amino, nitro, NH,  $\text{N}(\text{C}_1\text{-C}_3)$  straight chained or branched alkyl, O, S and  $\text{N}(\text{C}_1\text{-C}_4)$  straight chain or branched alkoxy; and,

pharmaceutically acceptable salts thereof.

36. A method according to Claim 35, wherein the non-antibiotic tetracycline compound selected from the group consisting of structures S-Z has the following provisos:

when either R7 and R9 are hydrogen then R8 must be halogen; and

when R6-a, R6, R5 and R9 are all hydrogen and R7 is hydrogen, amino, nitro, halogen, dimethylamino or diethylamino, then R8 must be halogen; and

when R6-a is methyl, R6 and R9 are both hydrogen, R5 is hydroxyl, and R7 is hydrogen, amino, nitro, halogen or diethylamino, then R8 is halogen; and

when R6-a is methyl, R6 is hydroxyl, R5, R7 and R9 are all hydrogen, then R8 must be halogen; and

when R6-a, R6 and R5 are all hydrogen, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

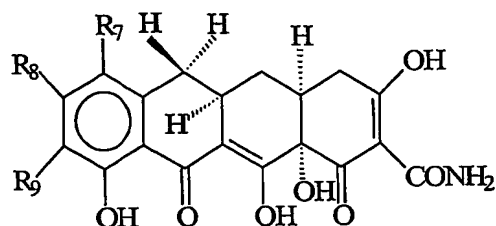
when R6-a is methyl, R6 is hydrogen, R5 is hydroxyl, R9 is methylamino and R7 is dimethylamino, then R8 must be halogen; and

when R6-a is methyl, R6, R5 and R9 are all hydrogen and R7 is cyano, then R8 must be halogen.

37. A method according to Claim 1, wherein said tetracycline compound has a photoirritancy factor of less than the photoirritancy factor of doxycycline.

38. A method according to Claim 1, wherein said tetracycline compound has a photoirritancy factor from about one to about two.

39. A method according to Claim 38, wherein said tetracycline compound has a general formula:

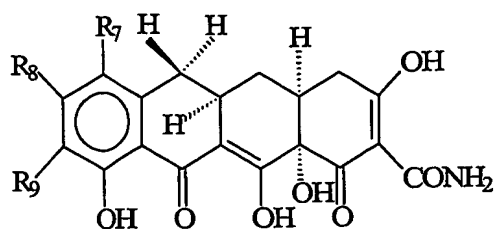


Structure K

wherein R7, R8, and R9 taken together are, respectively, hydrogen, hydrogen and dimethylamino.

40. A method according to Claim 1, wherein said tetracycline compound has a photoirritancy factor from about 1.0 to about 1.2.

41. A method according to Claim 41, wherein said tetracycline compound is selected from the group consisting of:



Structure K

wherein R7, R8, and R9 taken together in each case, have the following meanings:

R7

hydrogen  
hydrogen

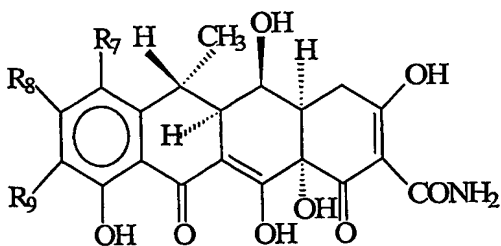
R8

hydrogen  
hydrogen

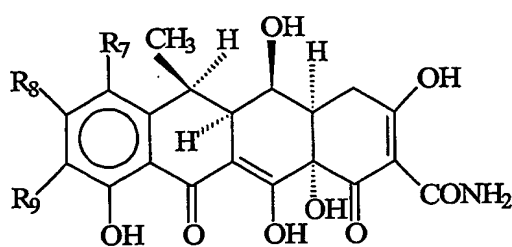
R9

amino  
palmitamide

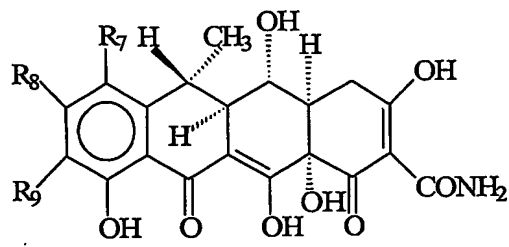
and



Structure L

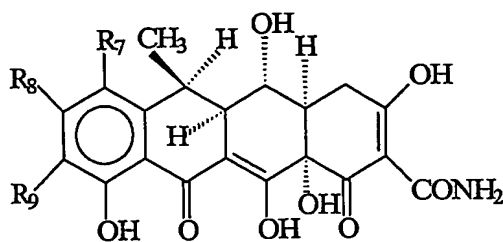


Structure M



Structure N

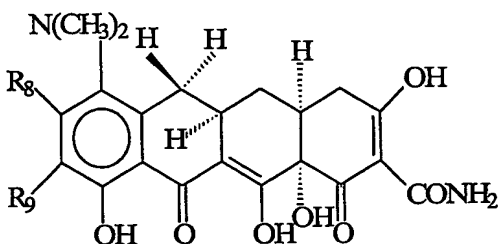




### Structure O

wherein R7, R8, and R9 taken together in each case, have the following meanings:

	R7	R8	R9
and	hydrogen	hydrogen	acetamido
	hydrogen	hydrogen	dimethylaminoacetamido
	hydrogen	hydrogen	nitro
	hydrogen	hydrogen	amino



**Structure P**

wherein R8, and R9 taken together are, respectively, hydrogen and nitro.

42. A method according to Claim 1 wherein said treatment comprises administering a non-antibiotic tetracycline derivative topically.
43. A method according to Claim 42 wherein said non-antibiotic tetracycline derivative is administered in a mouthwash.